

CLAIMS

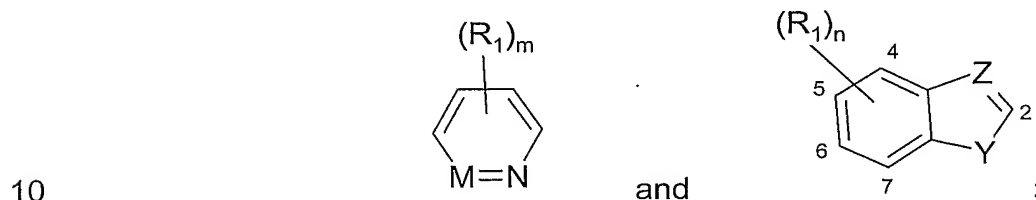
What is claimed is:

1. A method of treating a trichomoniasis infection in a subject in need thereof, the method comprising administering to the subject an effective amount of a compound of Formula (I):



wherein:

Ar_1 and Ar_2 are each independently selected from the group consisting of:



wherein:

M , N and Z are each independently selected from the group consisting of N and CH ;

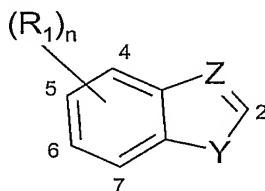
15 Y is selected from the group consisting of NR_3 , O , S , Se , and Te , wherein R_3 is selected from the group consisting of H , alkyl, and substituted alkyl;

each m is independently an integer from 0 to 2;

each n is independently an integer from 0 to 3;

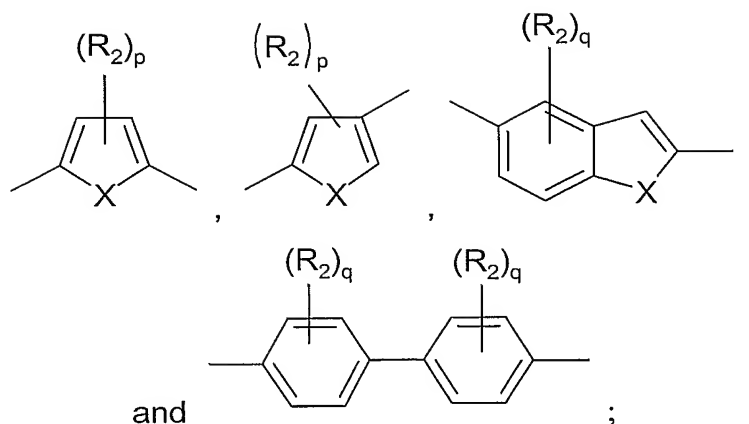
20 each R_1 is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxyl, aryl, substituted aryl, aryloxy, and aralkyloxy; and

wherein if Ar_1 or Ar_2 is:



Ar_1 or Ar_2 is attached to L through a bond at carbon 2;

25 L is selected from the group consisting of:



wherein:

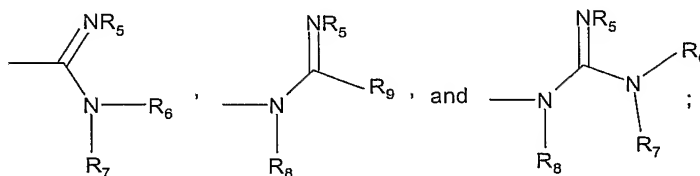
p is an integer from 0 to 2;

5 each q is independently an integer from 0 to 4;

X is selected from the group consisting of O, S, NR₄, Se, and Te, wherein R₄ is selected from the group consisting of H, alkyl, and substituted alkyl;

10 each R₂ is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxy, aryl, substituted aryl, aryloxy, and aralkyloxy; and

A₁ and A₂ are each independently selected from the group consisting of:



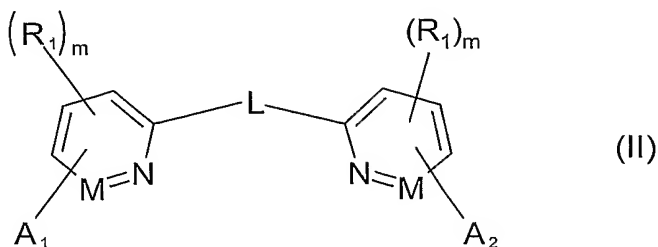
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wherein:

20 R₅, R₆, R₇, R₈, and R₉ are each independently selected from the group consisting of H, alkyl, substituted alkyl, cycloalkyl, aryl, substituted aryl, aralkyl, hydroxyl, alkoxy, hydroxyalkyl, hydroxycycloalkyl, alkoxycycloalkyl, aminoalkyl, acyloxy, alkylaminoalkyl, and alkoxycarbonyl; or

R₅ and R₆ together represent a C₂ to C₁₀ alkyl, C₂ to C₁₀ hydroxyalkyl, or C₂ to C₁₀ alkylene;
or a pharmaceutically acceptable salt thereof.

2. The method of Claim 1, wherein the compound of Formula (I) comprises a compound of Formula (II):



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wherein:

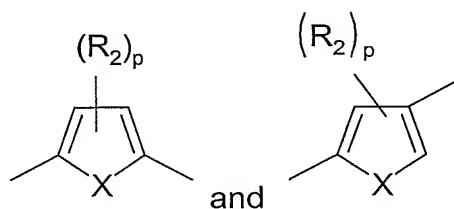
each M and N is independently selected from the group consisting of N and CH;

each m is independently an integer from 0 to 2;

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each R_1 is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxyl, aryl, substituted aryl, aryloxy, and aralkyloxy;

L is selected from the group consisting of:



wherein:

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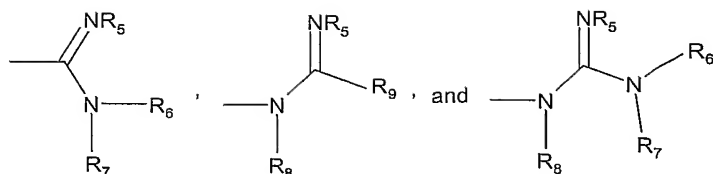
p is an integer from 0 to 2;

each R_2 is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxyl, aryl, substituted aryl, aryloxy, and aralkyloxy;

20

X is selected from the group consisting of O, S, NR_4 , Se, and Te, wherein R_4 is selected from the group consisting of H, alkyl, and substituted alkyl; and

A_1 and A_2 are each independently selected from the group consisting of:



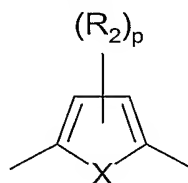
wherein:

R₅, R₆, R₇, R₈, and R₉ are each independently selected from the group consisting of H, alkyl, substituted alkyl, cycloalkyl, aryl, substituted aryl, aralkyl, hydroxyl, alkoxyl, hydroxyalkyl, hydroxycycloalkyl, alkoxyalkyl, aminoalkyl, acyloxy, alkylaminoalkyl, and alkoxyalkyl; or

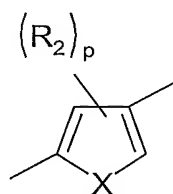
R₅ and R₆ together represent a C₂ to C₁₀ alkyl, C₂ to C₁₀ hydroxyalkyl, or C₂ to C₁₀ alkylene;

or a pharmaceutically acceptable salt thereof.

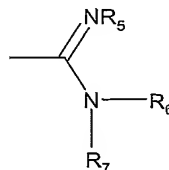
3. The method of Claim 2, wherein M and N are each CH.
4. The method of Claim 2, wherein L comprises:



5. The method of Claim 2, wherein L comprises:

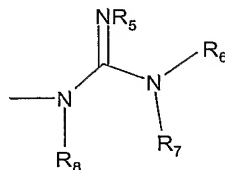


6. The method of Claim 2, wherein X is oxygen.
7. The method of Claim 2, wherein A₁ and A₂ each comprise:



and wherein R_6 and R_7 are independently selected from the group consisting of H, alkyl, substituted alkyl, and cycloalkyl; and R_5 is selected from the group consisting of H, hydroxyl, and alkoxy.

8. The method of Claim 2, wherein A_1 and A_2 each comprise:

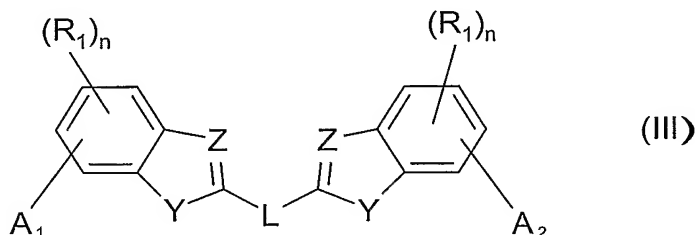


and wherein R_5 , R_6 , R_7 , and R_8 are each H.

9. The method of Claim 2, wherein the compound is selected from the group consisting of:

2,5-Bis(4-amidinophenyl)furan;
 2,5-Bis[4-(O-methoxyamidino)phenyl]furan;
 2,5-Bis[4-(N-isopropylamidino)phenyl]furan;
 2,5-Bis[4-(N-cyclohexylamidino)phenyl]furan;
 2,5-Bis(4-guanidinophenyl)furan; and
 3,5-Bis(4-amidinophenyl)furan.

10. The method of Claim 1, wherein the compound of Formula (I) comprises a compound of Formula (III):



wherein:

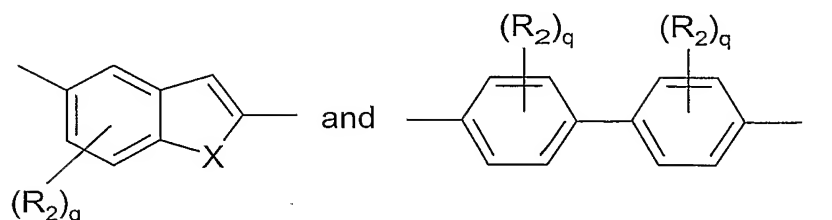
Y is selected from the group consisting of NR_3 , O, S, Se, and Te, wherein R_3 is selected from the group consisting of H, alkyl, and substituted alkyl;

Z is selected from the group consisting of CH and N;

each n is independently an integer from 0 to 3;

each R_1 is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxy, aryl, substituted aryl, aryloxy, and aralkyloxy;

L is selected from the group consisting of:



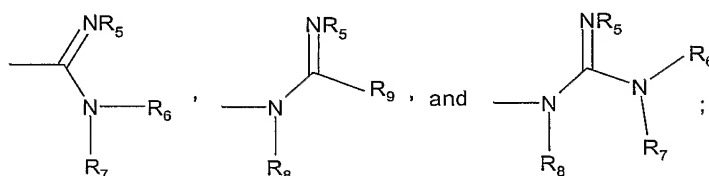
wherein:

X is selected from the group consisting of O, S, NR₄, Se, and Te, wherein R₄ is selected from the group consisting of H, alkyl, and substituted alkyl;

each q is independently an integer from 0 to 4;

each R₂ is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxy, aryl, substituted aryl, aryloxy, and aralkyloxy; and

A₁ and A₂ are each independently selected from the group consisting of:



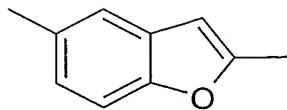
wherein:

R₅, R₆, R₇, R₈, and R₉ are each independently selected from the group consisting of H, alkyl, substituted alkyl, cycloalkyl, aryl, substituted aryl, aralkyl, hydroxyl, alkoxy, hydroxyalkyl, hydroxycycloalkyl, alkoxycycloalkyl, aminoalkyl, acyloxy, alkylaminoalkyl, and alkoxy carbonyl; or

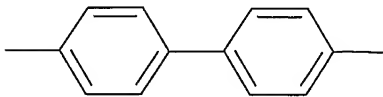
R₅ and R₆ together represent a C₂ to C₁₀ alkyl, C₂ to C₁₀ hydroxyalkyl, or C₂ to C₁₀ alkylene; or a pharmaceutically acceptable salt thereof.

11. The method of Claim 10, wherein Y is NH and Z is N.

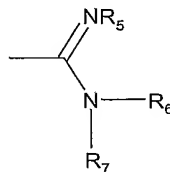
12. The method of Claim 10, wherein L comprises:



13. The method of Claim 10, wherein L comprises:



14. The method of Claim 10, wherein each A_1 and A_2 comprise

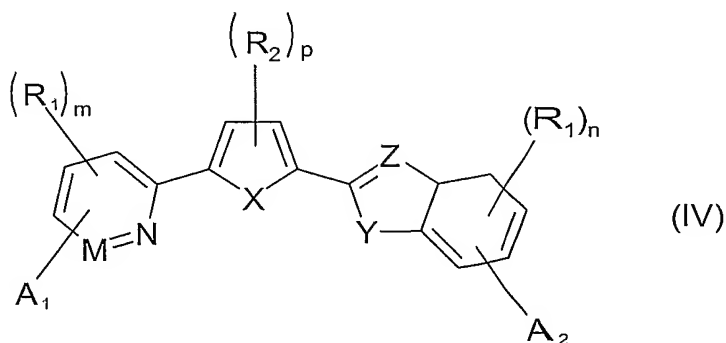


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and wherein R_6 and R_7 are independently selected from the group consisting of H, alkyl, substituted alkyl, and cycloalkyl; and R_5 is selected from the group consisting of H, hydroxyl, and alkoxy.

15. The method of Claim 10, wherein the compound is selected from the group consisting of 4,4'-Bis{2-[(4-amidino)benzimidazol]}biphenyl and 2,5-Bis{2-[5-(*N*-isopropylamidino)benzimidazol]}benzo[b]furan.

16. The method of Claim 1, wherein the compound of Formula (I) comprises a compound of Formula (IV):



15

wherein:

M , N and Z are each independently selected from the group consisting of N and CH;

Y is selected from the group consisting of NR₃, O, S, Se, and Te, wherein R₃ is selected from the group consisting of H, alkyl, and substituted alkyl;

m is an integer from 0 to 2;

5 n is an integer from 0 to 3;

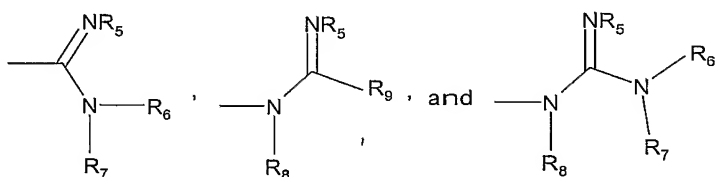
p is an integer from 0 to 2;

each R₁ and R₂ is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxy, aryl, substituted aryl, aryloxy, and aralkyloxy;

10 X is selected from the group consisting of O, S, NR₄, Se, and Te, wherein R₄ is selected from the group consisting of H, alkyl, and substituted alkyl; and

A₁ and A₂ are each independently selected from the group consisting of:

15



wherein:

20 R₅, R₆, R₇, R₈, and R₉ are each independently selected from the group consisting of H, alkyl, substituted alkyl, cycloalkyl, aryl, substituted aryl, aralkyl, hydroxyl, alkoxy, hydroxyalkyl, hydroxycycloalkyl, alkoxycycloalkyl, aminoalkyl, acyloxy, alkylaminoalkyl, and alkoxy carbonyl; or

25 R₅ and R₆ together represent a C₂ to C₁₀ alkyl, C₂ to C₁₀ hydroxyalkyl, or C₂ to C₁₀ alkylene;

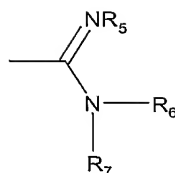
or a pharmaceutically acceptable salt thereof.

17. The method of Claim 16, wherein M and N are each CH.

18. The method of Claim 16, wherein Y is NH and Z is N.

19. The method of Claim 16, wherein X is sulfur.

30 20. The method of Claim 16, wherein A₁ and A₂ each comprise:



wherein R₅, R₆ and R₇ are each H.

21. The method of Claim 16, wherein the compound is 2-(4-Amidinophenyl)-5-[2-(5-amidinobenzimidazolyl)]thiophene.

22. The method of Claim 1, wherein the trichomoniasis infection is caused by the protozoan parasite *Trichomonas vaginalis*.

23. The method of Claim 1, wherein the compound of Formula (I) comprises a prodrug.

24. The method of Claim 1, wherein the compound of Formula (I) is administered in the form of a pharmaceutically acceptable salt.

25. The method of Claim 24, wherein the pharmaceutically acceptable salt comprises a hydrochloride salt.

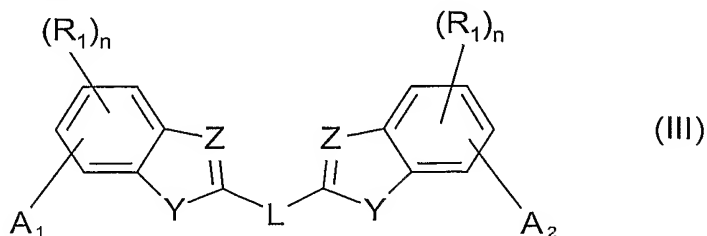
26. The method of Claim 1, wherein the subject is a human.

27. The method of Claim 1, comprising administering the compound of Formula (I) orally in one of a solid or a liquid formulation.

28. The method of Claim 1, comprising administering the compound in a liposomal formulation.

29. The method of Claim 1, comprising administering the compound of Formula (I) to prevent or reduce the incidence of recurrence of the *T. vaginalis* infection.

30. A compound of Formula (III):



wherein:

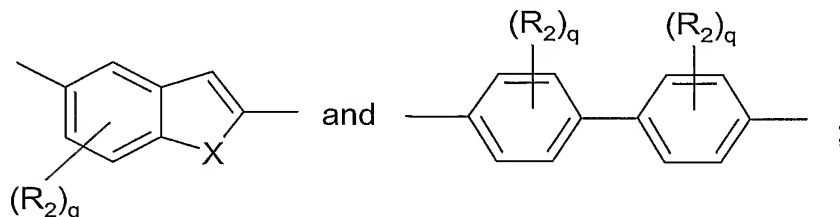
Y is selected from the group consisting of NR₃, O, S, Se, and Te, wherein R₃ is selected from the group consisting of H, alkyl, and substituted alkyl;

Z is selected from the group consisting of CH and N;

each n is independently an integer from 0 to 3;

each R₁ is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxyl, aryl, substituted aryl, aryloxy, and aralkyloxy;

L is selected from the group consisting of:



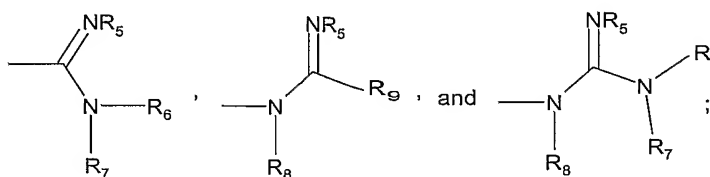
wherein:

X is selected from the group consisting of O, S, NR₄, Se, and Te, wherein R₄ is selected from the group consisting of H, alkyl, and substituted alkyl;

each q is independently an integer from 0 to 4;

each R₂ is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxyl, aryl, substituted aryl, aryloxy, and aralkyloxy; and

A₁ and A₂ are each independently selected from the group consisting of:



wherein:

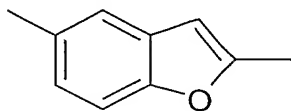
R₅, R₆, R₇, R₈, and R₉ are each independently selected from the group consisting of H, alkyl, substituted alkyl, cycloalkyl, aryl, substituted aryl, aralkyl, hydroxyl, alkoxyl, hydroxyalkyl, hydroxycycloalkyl, alkoxycycloalkyl, aminoalkyl, acyloxy, alkylaminoalkyl, and alkoxycarbonyl; or

R₅ and R₆ together represent a C₂ to C₁₀ alkyl, C₂ to C₁₀ hydroxyalkyl, or C₂ to C₁₀ alkylene;

or a pharmaceutically acceptable salt thereof.

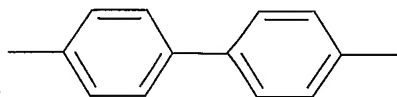
31. The compound of Claim 30, wherein Z is N and Y is NH.

32. The compound of Claim 30, wherein L comprises:

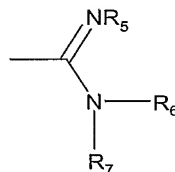


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33. The compound of Claim 30, wherein L comprises:



34. The compound of Claim 30 wherein A₁ and A₂ each comprise:



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wherein R₆ and R₇ are independently selected from the group consisting of H, alkyl, substituted alkyl and cycloalkyl; and R₅ is selected from the group consisting of H, hydroxyl, and alkoxy.

35. The compound of Claim 30, wherein the compound is selected from the group consisting of 4,4'-Bis{2-[(4-amidino)benzimidazolyl]}biphenyl, 2,5-Bis{2-[5-(*N*-isopropylamidino)benzimidazolyl]}benzo[*b*]furan, and pharmaceutically acceptable salts thereof,

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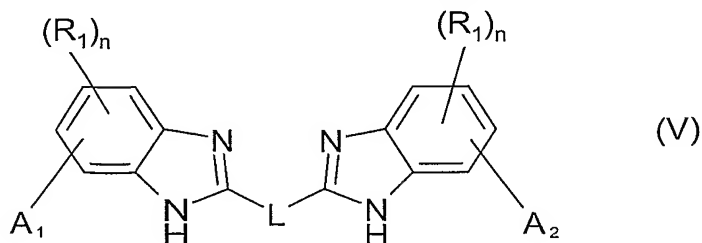
36. A compound of Claim 30, wherein the pharmaceutically acceptable salt is a hydrochloride salt.

37. A pharmaceutical formulation comprising:

- (a) a compound of Formula (III); and
- (b) a pharmaceutically acceptable carrier.

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38. A method of preparing a compound of Formula (V):

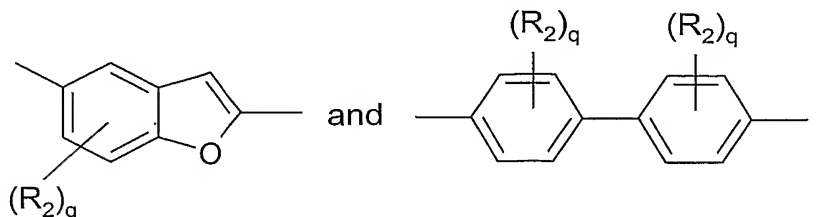


wherein:

each n is independently an integer from 0 to 3;

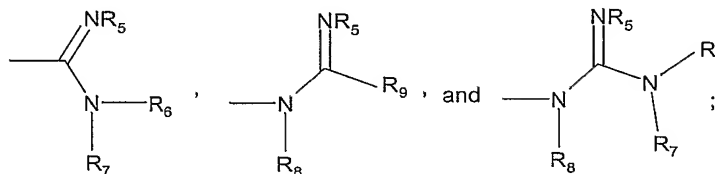
each R₁ is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxy, aryl, substituted aryl, aryloxy, and aralkyloxy;

L is selected from the group consisting of:



wherein each q is independently an integer from 0 to 4 and each R₂ is independently selected from the group consisting of alkyl, substituted alkyl, halo, hydroxyl, alkoxy, aryl, substituted aryl, aryloxy, and aralkyloxy; and

A₁ and A₂ are each independently selected from the group consisting of:



wherein:

R₅, R₆, R₇, R₈, and R₉ are each independently selected from the group consisting of H, alkyl, substituted alkyl, cycloalkyl, aryl, substituted aryl, aralkyl, hydroxyl, alkoxy, hydroxyalkyl, hydroxycycloalkyl, alkoxycycloalkyl, aminoalkyl, acyloxy, alkylaminoalkyl, and alkoxy carbonyl; or

R₅ and R₆ together represent a C₂ to C₁₀ alkyl, C₂ to C₁₀ hydroxyalkyl, or C₂ to C₁₀ alkylene;

the method comprising refluxing a mixture of a dialdehyde, two molar equivalents of a diamine and two molar equivalents of an aromatizing reagent in a polar, protic solvent to form a compound of Formula (V).

39. The method of Claim 38, wherein the dialdehyde is selected

from the group consisting of 4,4'-diformyl-1,1'-biphenyl and benzo[b]furan-2,5-dicarboxaldehyde.

40. The method of Claim 38, wherein the diamine is selected from the group consisting of 4-amidino-1,2-phenylenediamine and 4-*N*-isopropylamidino-1,2-phenylenediamine.

41. The method of Claim 38, wherein the aromatizing reagent comprises 1,4-benzoquinone.

42. The method of Claim 38, wherein the polar, protic solvent comprises ethanol.

43. The method of Claim 38, comprising:
(a) dissolving the compound of Formula (V) in a solvent to form a reaction mixture; and
(b) treating the reaction mixture with a solvent saturated with HCl to form a hydrochloride salt of the compound of Formula (V).